

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for inactivating a hepatitis C virus (HCV) in a patient comprising administering to said patient a modified siRNA in an effective amount to inactivate said virus, wherein said modified siRNA targets an HCV nucleotide sequence selected from the group consisting of 3'-untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, and the sequence targeted by siRNA5.
2. (Currently Amended) The method of claim 1, wherein said modified siRNA is a 2' modified siRNA modified at the 2' position of at least one ribonucleotide.
3. (Withdrawn) The method of claim 2, wherein the modification is at the 2' position of at least one ribonucleotide of said siRNA.
4. (Currently Amended) The method of claim 2 3, wherein said modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.
5. (Original) The method of claim 4, wherein said fluoro-modification is a 2'-fluoro-modification or a 2',2'-fluoro-modification.
6. (Currently Amended) The method of claim 5, wherein at least one pyrimidines of said siRNA ~~are~~ is modified, and said at least one pyrimidines ~~are~~ is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
7. (Original) The method of claim 1, wherein both strands of said siRNA contain at least one modified nucleotide.
8. (Withdrawn) The method of claim 1, wherein said virus is selected from the group consisting of hepatitis C virus (HCV), hepatitis A virus, hepatitis B virus, hepatitis D virus, hepatitis E virus, Ebola virus, influenza virus, rotavirus, reovirus, retrovirus, poliovirus, human papilloma virus (HPV), metapneumovirus and coronavirus.

9. (Withdrawn) The method of claim 8, wherein said virus is hepatitis C virus.
10. (Currently Amended) The method of claim 1 8, wherein said siRNA is prepared by
- (a) identifying a target nucleotide sequence in ~~an HCV genome~~ 3'-untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, or the sequence targeted by siRNA5 for designing a small interfering RNA (siRNA); and
- (b) producing an siRNA that has been modified to contain at least one modified nucleotide.
11. (Withdrawn) The method of claim 8, wherein said siRNA is prepared by
- (a) identifying a target nucleotide sequence in a virus genome for designing a small interfering RNA (siRNA); and
- (b) producing an siRNA that has been modified to contain at least one modified nucleotide.
12. (Withdrawn) The method of claim 10, wherein said target nucleotide sequence is selected from the group consisting of 5'-untranslated region (5'-UTR), 3'-untranslated region (3'-UTR), core, and NS3 helicase.
13. (Currently Amended) The method of claim ~~12~~ 1 or 10, wherein said siRNA is siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.
14. (Currently Amended) ~~An~~ A modified siRNA comprising a at least one modified ribonucleotide, wherein said siRNA is resistant to RNase and retains the ability to inhibit hepatitis C virus (HCV) ~~viral~~ replication, and wherein said modified siRNA targets an HCV nucleotide sequence selected from the group consisting of 3'-untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, and the sequence targeted by siRNA5.

15. (Currently Amended) The modified siRNA of claim 14, wherein said modified siRNA is a 2' modified siRNA modified at the 2' position of at least one ribonucleotide.
16. (Withdrawn) The siRNA of claim 15, wherein the modification is at the 2' position of at least one ribonucleotide of said siRNA.
17. (Currently Amended) The modified siRNA of claim 14 15, wherein the modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.
18. (Currently Amended) The modified siRNA of claim 17, wherein said fluoro-modification is a 2'-fluoro-~~modification~~ or a 2',2'-fluoro-modification.
19. (Currently Amended) The modified siRNA of claim 18, wherein at least one pyrimidines of said siRNA ~~are~~ is modified, and said at least one pyrimidines ~~are~~ is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
20. (Currently Amended) The modified siRNA of claim 14, wherein both strands of the siRNA contains at least one modified nucleotides.
21. (Withdrawn) The siRNA of claim 14, wherein said siRNA interacts with a target nucleotide sequence in a virus genome.
22. (Withdrawn) The siRNA of claim 21, wherein said virus is selected from the group consisting of hepatitis C virus (HCV), hepatitis A virus, hepatitis B virus, hepatitis D virus, hepatitis E virus, Ebola virus, influenza virus, rotavirus, reovirus, retrovirus, poliovirus, human papilloma virus (HPV), metapneumovirus and coronavirus.
23. (Withdrawn) The siRNA of claim 22, wherein said virus is hepatitis C virus (HCV).
24. (Currently Amended) A method of making a modified siRNA that targets a nucleic acid sequence in a hepatitis C virus (HCV) comprising:
 - (a) preparing a modified-double stranded RNA (dsRNA) fragment containing at least one modified ribonucleotide in at least one strand that spans ~~the genome of a target agent~~ 3'

untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, or the sequence targeted by siRNA5; and

(b) cleaving said modified-dsRNA fragments with ~~recombinant human~~ Dicer resulting in ~~more than~~ at least one modified siRNA that targets an HCV nucleotide sequence selected from the group consisting of 3'-untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, and the sequence targeted by siRNA5.

25. (Currently Amended) The method of claim 24, further comprising:

(c) isolating said at least one modified siRNAs.

26. (Withdrawn) The method of claim 24, wherein said target agent is a virus.

27. (Withdrawn) The method of claim 26, wherein said virus is selected from the group consisting of hepatitis C virus (HCV), hepatitis A virus, hepatitis B virus, hepatitis D virus, hepatitis E virus, Ebola virus, influenza virus, rotavirus, reovirus, retrovirus, poliovirus, human papilloma virus (HPV), metapneumovirus and coronavirus.

28. (Currently Amended) A method for inactivating a hepatitis C virus (HCV) in a patient comprising administering to said patient a modified siRNA consisting of about 10 to about 30 ribonucleotides in an effective amount to inactivate said virus, wherein said modified siRNA targets an HCV nucleotide sequence selected from the group consisting of 3'-untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, and the sequence targeted by siRNA5.

29. (Original) The method of claim 28, wherein said modified siRNA consists of about 19 to about 23 ribonucleotides.

30. (Currently Amended) The method of claim 28, wherein said modified siRNA is a 2' modified siRNA modified at the 2' position of at least one ribonucleotide.

31. (Withdrawn) The method of claim 30, wherein the modification is at the 2' position of at least one ribonucleotide of said siRNA.
32. (Currently Amended) The method of claim ~~31~~ 30, wherein said modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.
33. (Original) The method of claim 32, wherein said fluoro-modification is a 2'-fluoro-modification or a 2',2'-fluoro-modification.
34. (Currently Amended) The method of claim ~~28~~ 33, wherein at least one pyrimidines of said siRNA ~~are~~ is modified and said at least one pyrimidines~~are~~ is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
35. (Currently Amended) The method of claim 28, wherein both strands of said siRNA contain at least one modified nucleotides.
36. (Withdrawn) The method of claim 28, wherein said virus is selected from the group consisting of hepatitis C virus (HCV), hepatitis A virus, hepatitis B virus, hepatitis D virus, hepatitis E virus, Ebola virus, influenza virus, rotavirus, reovirus, retrovirus, poliovirus, human papilloma virus (HPV), metapneumovirus and coronavirus.
37. (Withdrawn) The method of claim 36, wherein said virus is hepatitis C virus (HCV).
38. (Currently Amended) The method of claim ~~37~~ 28, wherein said siRNA is prepared by
- (a) identifying a target nucleotide sequence in a ~~HCV genome~~ 3'-untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, or the sequence targeted by siRNA5 for designing a small interfering RNA (siRNA); and
- (b) producing an siRNA that has been modified to contain at least one modified nucleotide.
39. (Withdrawn) The method of claim 36, wherein said siRNA is prepared by

(a) identifying a target nucleotide sequence in a virus genome for designing a small interfering RNA (siRNA); and

(b) producing an siRNA that has been modified to contain at least one modified nucleotide.

40. (Withdrawn) The method of claim 38, wherein said target nucleotide sequence comprises a conserved nucleotide sequence necessary for HCV replication.

41. (Withdrawn) The method of claim 40, wherein said conserved nucleotide sequence is selected from the group consisting of 5'-untranslated region (5'-UTR), 3'-untranslated region (3'-UTR), core, and NS3 helicase.

42. (Currently Amended) The method of claim 41 ~~28~~, wherein said siRNA is siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.

43. (Currently Amended) A double-stranded RNA molecule of from about 10 to about 30 nucleotides that inhibits replication of hepatitis C virus (HCV) and targets an HCV nucleotide sequence selected from the group consisting of 3'-untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, and the sequence targeted by siRNA5.

44. (Original) The double-stranded RNA molecule of claim 43 comprising a nucleotide sequence at least 80% identical to the nucleotide sequence of siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.

45. (Currently Amended) A method of inducing targeted RNA interference toward HCV in hepatic cells, comprising administering the double-stranded RNA molecule of claim 43 to hepatic cells, wherein the nucleotide sequence of said double-stranded RNA molecule corresponds to ~~an~~ the targeted HCV nucleotide sequence.

46. (Original) A method of inhibiting replication of hepatitis C virus (HCV), comprising administering the RNA polynucleotide molecule of claim 44 to cells infected with HCV.

47. (Original) A vector comprising a DNA segment encoding the RNA molecule of claim 43.

48. (Currently Amended) The vector of claim 47, wherein the sense strand of said double-stranded RNA molecule is operably linked to a first promoter and wherein the antisense strand of said double-stranded RNA molecule is operably linked to a second promoter.

49. (Original) The vector of claim 48, wherein said first and second promoters are selected from the group consisting of U6 and H1.

50. (Original) The vector of claim 48 wherein said first and second promoters are the same.

51. (Original) The vector of claim 47, wherein the sense and antisense strands of said RNA molecule are under the control of a single promoter.

52. (Original) The vector of claim 51, wherein said single promoter is selected from the group consisting of U6 and H1.

53. (Original) A host cell comprising the vector of claim 47.

54. (Original) A method of inhibiting replication of hepatitis C virus (HCV) in cells carrying HCV, comprising transfecting said cells with the vector of claim 47.

55. (Currently Amended) A method of treating hepatitis C in a subject in need thereof, comprising administering a composition comprising a therapeutically effective amount of the RNA molecule of claim 43 to said subject.

56. (Original) A method of treating hepatitis C in a subject in need thereof, comprising administering the vector of claim 47 to said subject.

57. (Currently Amended) A modified siRNA molecule, comprising a double-stranded RNA molecule of from about 10 to about 30 nucleotides in length, which mediates RNA interference toward ~~a target agent or virus~~ hepatitis C virus (HCV) and targets an HCV

nucleotide sequence selected from the group consisting of 3'-untranslated region (3'-UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, and the sequence targeted by siRNA5, and which is linked to at least one receptor-binding ligand.

58. (Original) The modified siRNA molecule of claim 57, wherein said receptor-binding ligand is attached to a 5'-end or 3'-end of said siRNA molecule.

59. (Original) The modified siRNA molecule of claim 58, wherein said receptor binding ligand is attached to multiple ends of said siRNA molecule.

60. (Original) The modified siRNA molecule of claim 57, wherein said receptor-binding ligand is selected from the group consisting of a cholesterol, an HBV surface antigen, low-density lipoprotein, an HIV-1 surface antigen, an influenza virus surface antigen, an RSV surface antigen, an HPV surface antigen and a polio virus surface antigen.

61. (Original) The modified siRNA molecule of claim 60, wherein said receptor-binding ligand is cholesterol.

62. (Original) The modified siRNA molecule of claim 57, further comprising a modification at the 2' position of at least one ribonucleotide, which modification at the 2' position of at least one ribonucleotide renders said siRNA resistant to degradation.

63. (Withdrawn) The modified siRNA molecule of claim 62, wherein said modification at the 2' position of at least one ribonucleotide is a 2'-fluoro-modification or a 2',2'-fluoro-modification.

64. (Original) A method of inducing targeted RNA interference in a patient, comprising administering to said patient an effective amount of the siRNA of claim 57.

65. (Original) A method of inducing targeted RNA interference in a patient, comprising administering to said patient an effective amount of the siRNA of claim 61.

66. (Original) A method of inducing targeted RNA interference in a patient, comprising administering to said patient an effective amount of the siRNA of claim 63.

67. (Newly Added) The method of claim 1, wherein said modified siRNA is modified in at least one nucleotide base.
68. (Newly Added) The method of claim 67, wherein at least one pyrimidine of said siRNA is modified, and said at least one pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
69. (Newly Added) The method of claim 1, wherein said modified siRNA is modified in at least one phosphate linkage.
70. (Newly Added) The modified siRNA of claim 14, wherein said modified siRNA is modified in at least one nucleotide base.
71. (Newly Added) The modified siRNA of claim 70, wherein at least one pyrimidine of said siRNA is modified, and said at least one pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
72. (Newly Added) The modified siRNA of claim 14, wherein said modified siRNA is modified in at least one phosphate linkage.
73. (Newly Added) The method of claim 28, wherein said modified siRNA is modified in at least one nucleotide base.
74. (Newly Added) The method of claim 73, wherein at least one pyrimidine of said siRNA is modified, and said at least one pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
75. (Newly Added) The method of claim 28, wherein said modified siRNA is modified in at least one phosphate linkage.
76. (Newly Added) The modified siRNA molecule of claim 62, wherein said 2'-modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.

77. (Newly Added) The modified siRNA molecule of claim 76, wherein said fluoro-modification is a 2'-fluoro-modification or a 2',2'-fluoro-modification.
78. (Newly Added) The modified siRNA molecule of claim 57, wherein said modified siRNA is modified in at least one nucleotide base.
79. (Newly Added) The modified siRNA molecule of claim 78, wherein at least one pyrimidine of said siRNA is modified, and said at least one pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
80. (Newly Added) The modified siRNA molecule of claim 57, wherein said modified siRNA is modified in at least one phosphate linkage.
81. (Newly Added) The modified siRNA of claim 14 comprising a nucleotide sequence at least 80% identical to the nucleotide sequence of siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.